REMARKS

The Amendment, filed in response to the Office Action mailed January 15, 2009, is believed to be fully responsive to all issues raised in the Action. Entry of the amendment and favorable reconsideration of the application is respectfully requested.

Claims Disposition and Summary of Amendments

Claims 1-13 are all the claims pending in the application. Claims 11-13 are withdrawn from consideration as being drawn to non-elected invention. Claims 1-10 were considered and all stand rejected.

Upon entry of the amendment, which is respectfully requested, claim 1 will be amended to more clearly set forth the feature of the claimed subject matter. Support for the amended claim may be found by the disclosure, for example at page 3, lines 12-14, page 4, lines 6-9, page 5, lines 4-8, and the like of the specification. No new matter is introduced.

Formal Matters and Withdrawn Rejections/Objections

Applicant notes that the Office Action Summary, boxes 4 and 6 incorrectly indicate claims 10-13 are withdrawn and claims 1-9 are considered. As the Detailed Action correctly indicates claims 1-10 are considered and claims 11-13 are withdrawn. A correct indication of claims disposition in a next Office Action is respectfully requested.

Applicant thanks the Examiner for withdrawing previous rejections and objections in view of Applicant's arguments and/or amendments.

Response to Rejection under 35 U.S.C. § 103

In the Action, claims 1-9 stand rejected under 35 U.S.C. 103(a) as assertedly being unpatentable over Patel et al. (US Pre-Grant Publication 2003/0064097) ("Patel") in combination with Kawamura et al. (US Pre-Grant Publication 2004/0219208) ("Kawamura").

Claim 10 stands rejected under 35 U.S.C. 103(a) as assertedly being unpatentable over the combined teachings of Patel and Kawamura as set forth above with respect to claim 1 in combination with Nielsen et al. (USPN 5,716,558) ("Nielsen").

The Office asserts that Patel teaches methods for preparing multiparticulate compositions using processes which comprise applying an encapsulation coat onto a substrate (e.g. spray coating and nanoencapsulation) as well as collection of the ensuing particles [0223]. According to the Office, preparation of the encapsulation coating solution is taught as solubilizing or suspending a composition in a mixture comprising an organic solvent and a supercritical fluid, and which can further comprise additives and paragraph [0257] of Patel specifically teaches that multiple organic solvents may be combined as the organic solvent of the coating solutions.

The Office recognizes that Patel does not expressly teach removal (e.g. displacement) of the mixed organic solvent portion of the dispersing medium by washing the coated particles with additional supercritical fluid, nor does Patel expressly teaches Applicants' instantly claimed polymer/active weight ratio, percent range of the hydrophilic polymer or the weight ratio of the two organic solvents mixed.

The Office resorts Kawamura as teaching a process for preparing a sustained-release preparation comprising injectable microcapsules or microspheres [0225] and [0226] which comprises an AII antagonist and an anticancer drug (Abstract; claim 1).

It is the Office's position that it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare a nano-scale paclitaxcl solid dispersion (e.g. suspension) by contacting a paclitaxel/additive/mixed alcohol solvent solution with a supercritical fluid, displacing said alcohol solvent with supercritical fluid and recover the resulting particles, as taught and suggested by the combined teachings of Patel and Kawamura.

With respect to claim 10, the Office states that neither Patel nor Kawamura teach the temperature or pressure application parameters for the supercritical fluid as set forth by Applicants in claim 10. Nielsen is relied upon as teaching methods for spraying liquid compositions by using compressed fluids such as carbon dioxide, to form solid particulates and coating powders which may be produced with narrow particle size distributions (Abstract); and further teaching that compressed carbon dioxide fluid may be sprayed at a temperature of 60°C and a pressure of 1600 pounds/sq. inch (1 bar/14.5 psi) or about 110.3 bar (col. 13, lines 19-26).

The Office asserts that it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to have sprayed a supercritical fluid (e.g. carbon dioxide) using Applicants' instantly claimed physical parameters in view of Nielsen's teaching that application of a supercritical fluid to a liquid water-borne polymeric composition comprising a mixed organic solvent produced a dry, collectable powder (Example 9).

Applicant respectfully traverses for the following reasons.

<u>One skilled in the art would not have been motivated to combine references</u>

Applicant respectfully submits that a person ordinary skilled in the art would not be motivated to combine Patel and Kawamura since their objects are clearly different from each other.

Specifically, the object of Patel is improving the solubility of hydrophobic active ingredients in order to improve delivery of the hydrophobic active ingredients, while Kawamura relates to releasing drugs in sustained manner. The increase in solubility of an active ingredient means that the active ingredient can dissolve into a biological fluid such as gastric juice better and faster, thereby increasing the bioavailability of the active ingredient in vivo. On the other hand, sustained release is a kind of time release technology employed in formulating a medicine in order to have a drug dissolve slowly and release a drug over time (*see* "http://en.wikipedia.org/wiki/ Sustained_release" ("in sustained release … formulated to dissolve slowly and release a drug over time").

No guidance to choose and combine paclitaxel and supercritical fluid process

In addition, the subject invention improves the solubility of, especially, paclitaxel, by using a supercritical fluid, thereby changing the crystallinity of paclitaxel. That is, the feature of the subject invention resides in the unique combination of a drug and a process for forming a solid dispersion thereof.

However, according to Patel, paclitaxel is embedded in a boilerplate list of pharmaceutically active ingredients, and there is no working example confirming an improved solubility of a composition comprising paclitaxel; and Kawamura only teaches that removal of water and organic solvent using supercritical fluid. Further, both of the cited references fail to disclose any relationship between solubility and crystallinity of a drug changed by using a supercritical fluid.

Thus, Patel and Kawamura fail to disclose or suggest that, when using supercritical fluid method among numerous methods for preparing a solid dispersion, the solubility of paclitaxel

among such a large number of drugs can be remarkably improved by the change of crystallinity of paclitaxel.

Accordingly, even if they are combined together, a person skilled in the art would not have been able to select paclitaxel and supercritical fluid method and conceive the unique process for the improvement of paclitaxel solid dispersion of the subject invention.

Claimed invention shows unexpectedly remarkable effects

Moreover, the effects stemming from the unique combination of paclitaxel and a supercritical fluid are recognized as unexpectedly remarkable compared with those of the cited reference. Specifically, the solubilities of paclitaxel solid dispersions prepared by the supercritical fluid process of the subject invention are remarkably higher (about 3,000 times) than that of the solid dispersion prepared by using liquid carbon dioxide or a conventional paclitaxel powder (see Table 25 of the subject specification). In contrast, although the compositions are not for paclitaxel, the dissolution ratios of the glyburide composition in Example 2 and the progestetone composition in Example 3 of Patel show merely 2 and 3 times higher than that of the pure bulk drug (see Figures 1, 2A and 2B of Patel). Furthermore, the amounts of surfactants (e.g., Myrj 52) comprised in the composition for further improving solubility of the subject invention, i.e., 2.5 to 25g, is much lower than those employed in Examples 2 to 5, and 13 to 28 of Patel.

Accordingly, the subject invention defined in claims 1 to 9 and claim 10 reciting claim 1 is evidently patentable and unobvious over the cited references. Withdrawal of the rejections is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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